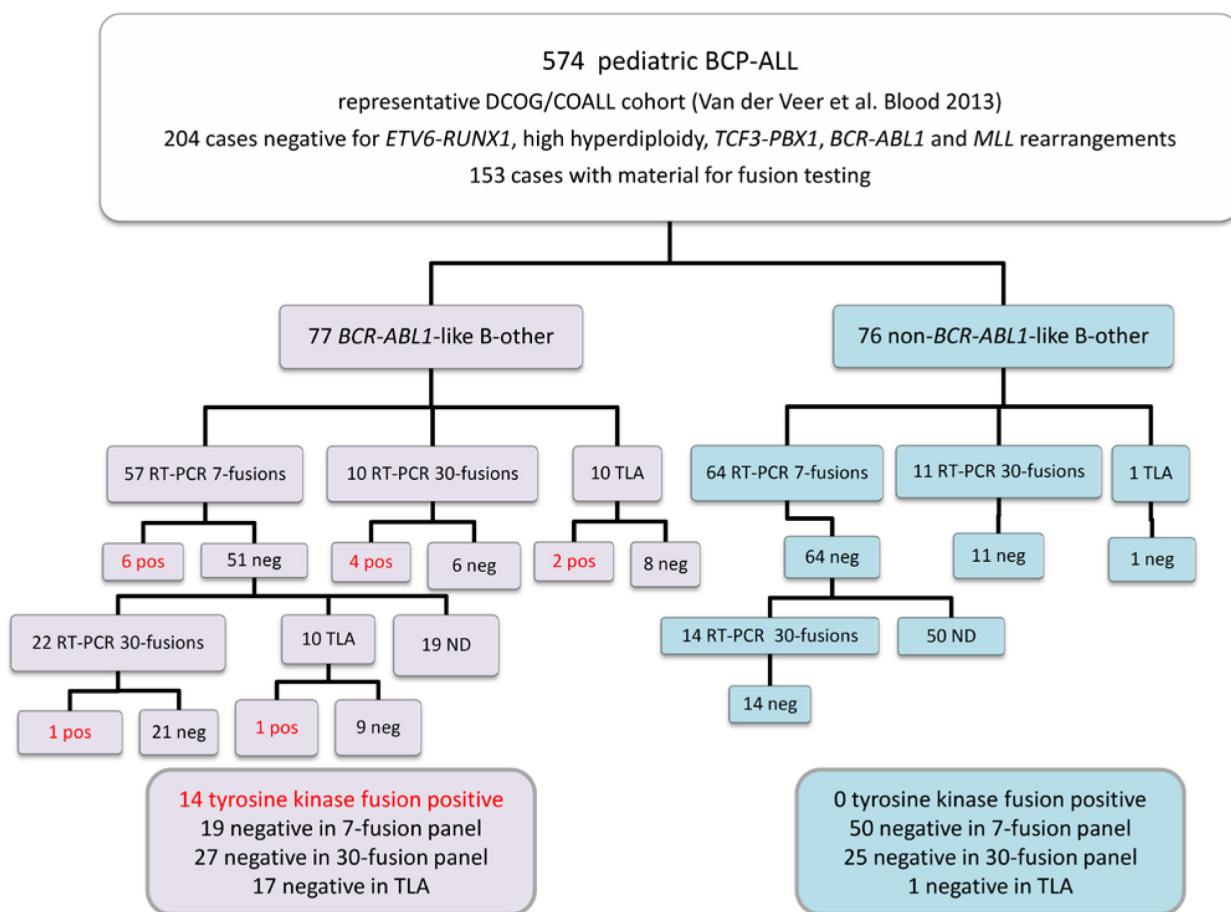
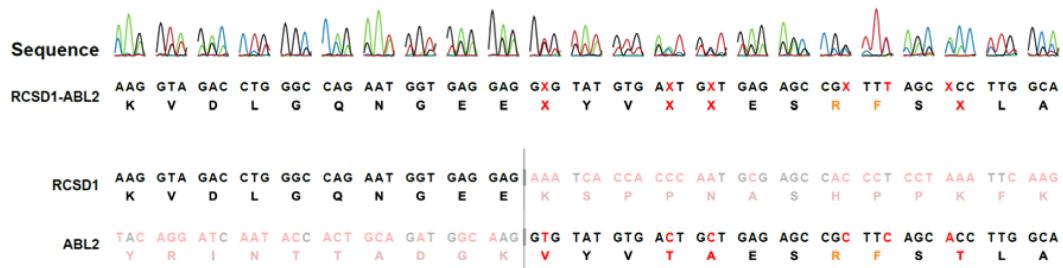
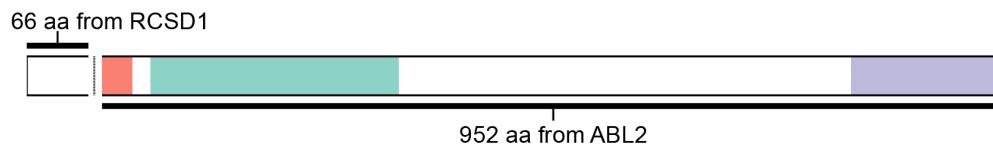


## Tyrosine kinase fusion genes in pediatric *BCR-ABL1*-like acute lymphoblastic leukemia

### SUPPLEMENTARY DATA

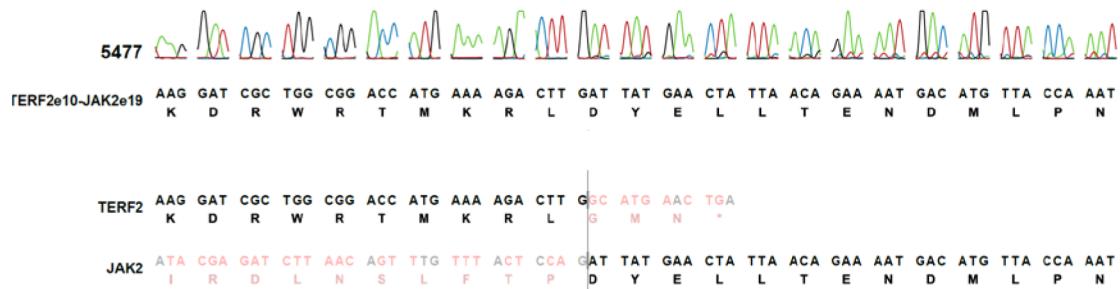


**Supplementary Figure 1: Overview of cohort screened for tyrosine kinase fusion genes.** Flowchart showing the number of cases tested for tyrosine kinase fusion genes using an RT-PCR panel of 7 fusions [3], an RT-PCR panel of 30 fusions [1], and targeted locus amplification for 6 kinases [4]. Boxes at the bottom summarize the number of positive and negative cases per method. ND, not determined.

**A****B****C**

AACTAGGGCTCCCTGCTCCCTTACTGAGGCTCTTATGATTGTCAAGGACACGAACACTATTTCAA  
GCCTGAGAGAACAGAAAATTGATAATTTCACAAGTAGATACTTTATACACTAAAACAAAAGCTTTTTT  
TTT

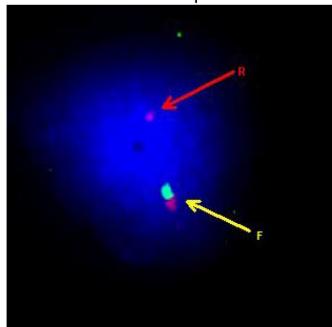
**Supplementary Figure 2: Sanger sequencing and TLA fusion read of *RCSD1-ABL2* in case A530.** **A.** Sequence confirmation of the *RCSD1-ABL2* fusion by Sanger sequencing of RT-PCR product indicates fusion of *RCSD1* exon 3 to *ABL2* exon 5. For primers used in validation RT-PCR see Supplementary Table S2. The fusion encodes an in frame fusion protein. **B.** Schematic representation of the in-frame *RCSD1-ABL2* fusion protein drawn in ProteinPaint [5]. **C.** Targeted locus amplification genomic DNA fusion read showing *RCSD1* intron 3 (chr1) (red) and *ABL2* intron 4 (chr1) in green.

**A****B**

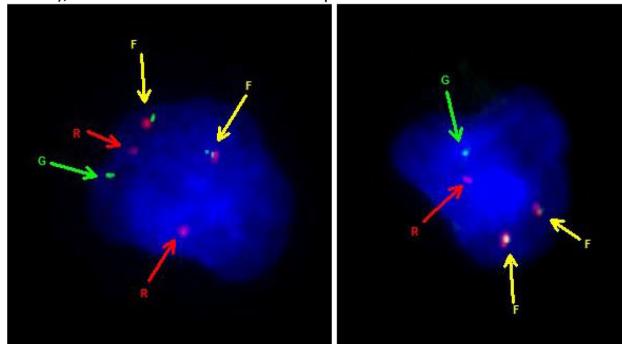
**Supplementary Figure 3: Sanger sequencing of *TERF2-JAK2* in case A214.** **A.** Sequence confirmation of the *TERF2-JAK2* fusion by Sanger sequencing of RT-PCR product indicates fusion of *TERF2* exon 10 to *JAK2* exon 19. For primers used in validation RT-PCR see Supplementary Table S2. The fusion encodes an in frame fusion protein. **B.** Schematic representation of the in-frame *TERF2-JAK2* fusion protein drawn in ProteinPaint [5].

**(A) PDGFRB R32**

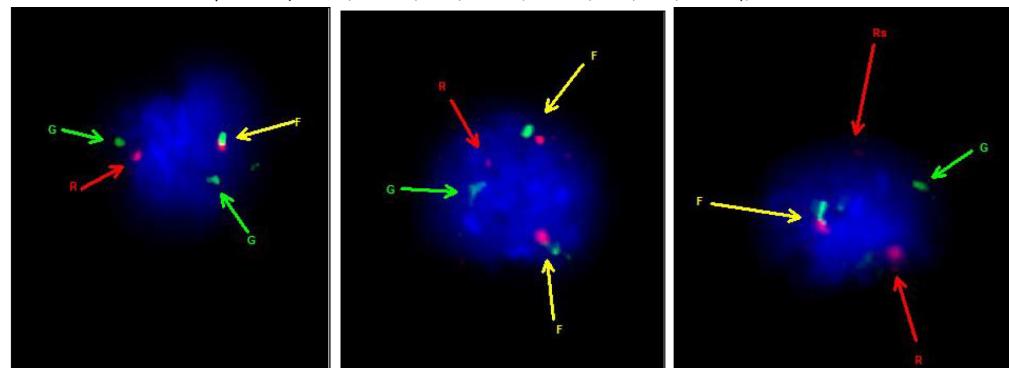
83% with unbalanced pattern with one normal locus and loss of telomeric probe (Fusion, Red)

**(B) PDGFRB A288**

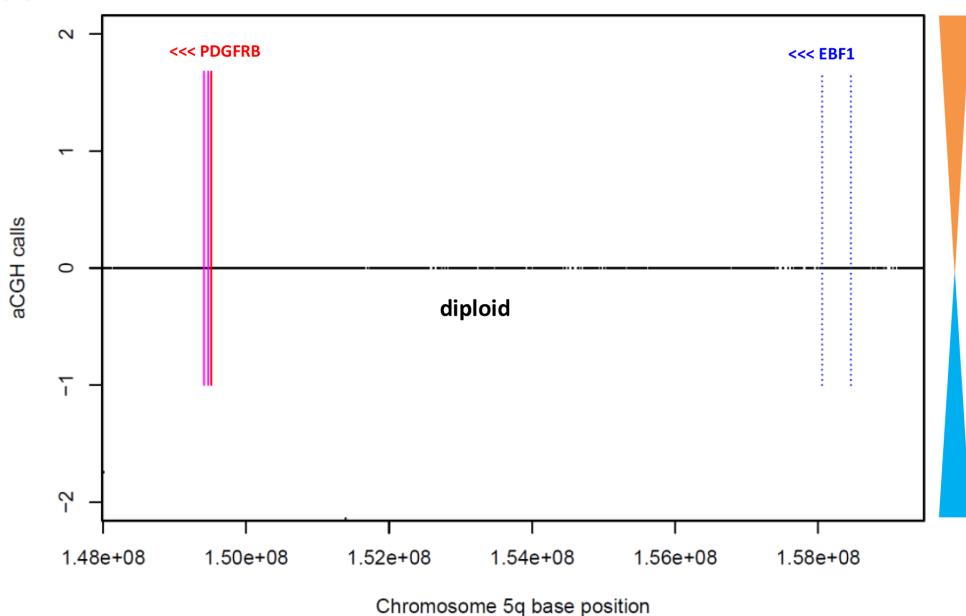
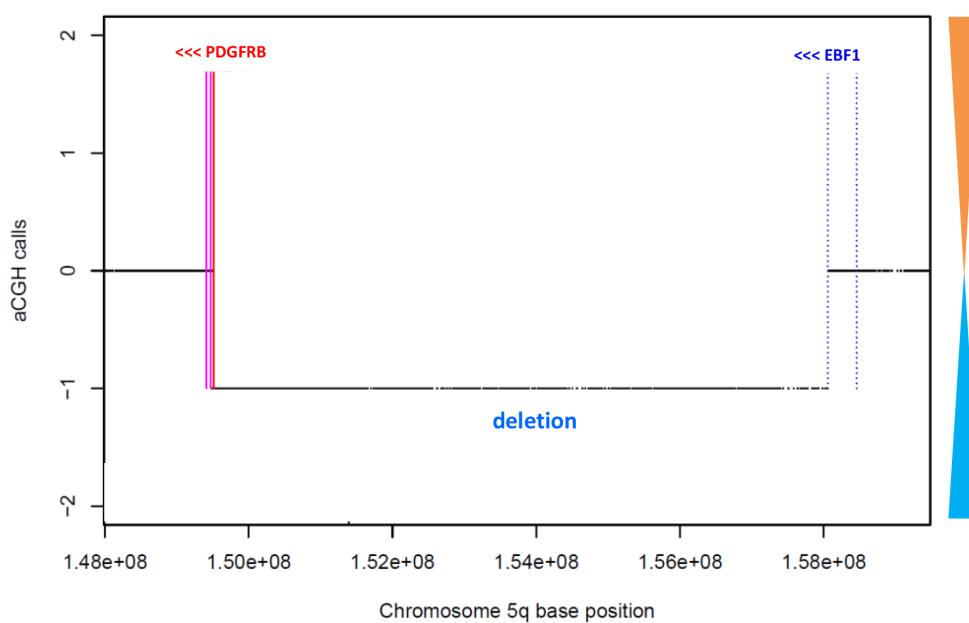
32% with balanced translocation and two normal loci (Fusion, Fusion, Red, Green);  
 56% with balanced pattern and two normal loci and an additional signal for centromeric probe (Fusion, Fusion, Red, Red, Green); also some smaller subclones present

**(C) PDGFRB A428**

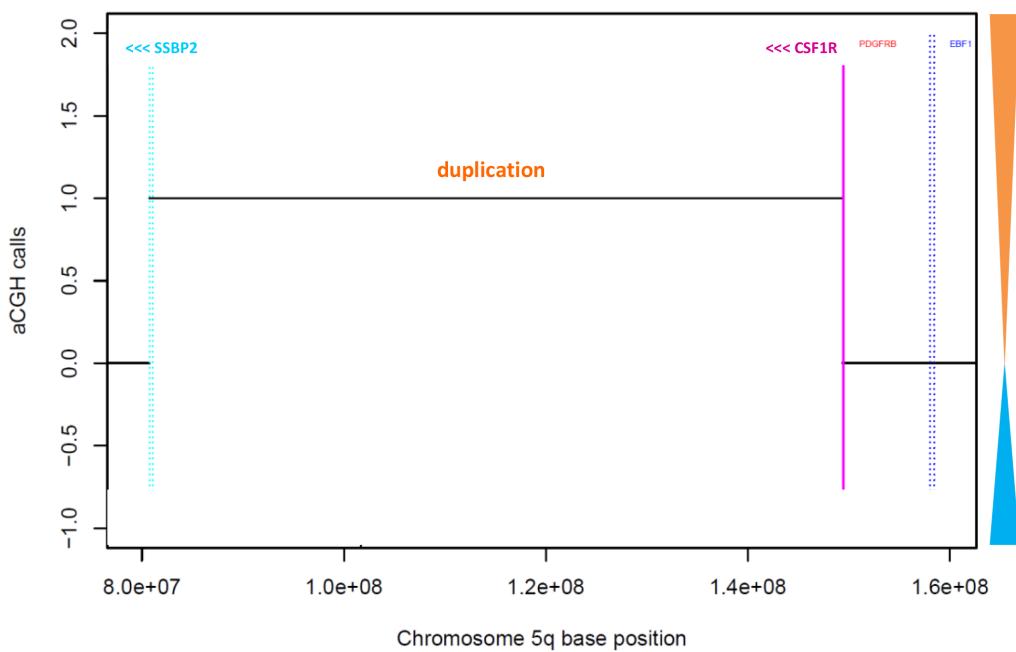
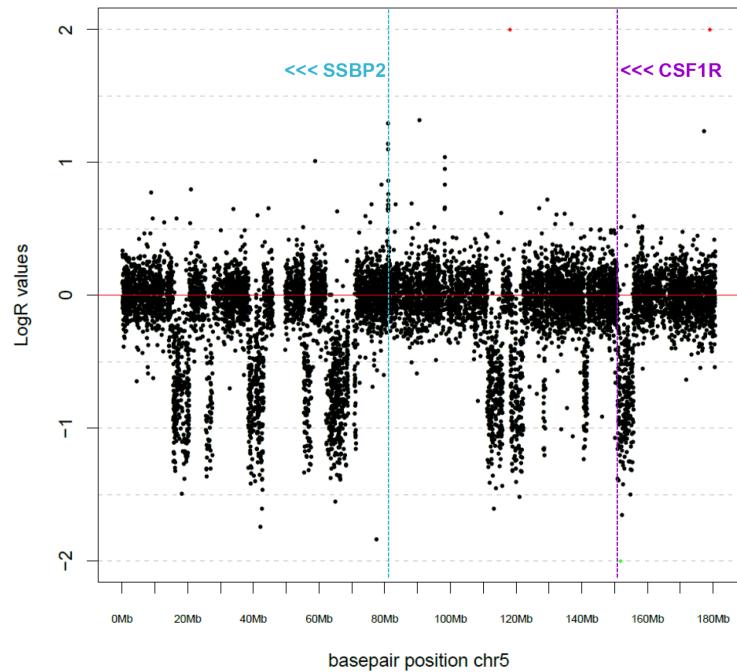
22% balanced pattern with one normal locus (Fusion, Red, Green);  
 64% balanced pattern with one normal locus and one additional signal for telomeric probe (Fusion, Red, Green, Green);  
 some smaller subclones present (Fusion, Fusion, Red, Green; Fusion, Red, Red, Green);



**Supplementary Figure 4: FISH with *PDGFRB* break apart probes on *EBF1-PDGFRB* fusion cases.** FISH probes were from Cytocell, centromeric probe red, telomeric probe green. **A.** *PDGFRB* R32. 83% with unbalanced pattern with one normal locus and loss of telomeric probe (Fusion, Red). **B.** *PDGFRB* A288. 32% with balanced translocation and two normal loci (Fusion, Fusion, Red, Green); 56% with balanced pattern and two normal loci and an additional signal for centromeric probe (Fusion, Fusion, Red, Red, Green); also some smaller subclones present. **C.** *PDGFRB* A428. 22% balanced pattern with one normal locus (Fusion, Red, Green); 64% balanced pattern with one normal locus and one additional signal for telomeric probe (Fusion, Red, Green, Green); some smaller subclones present (Fusion, Fusion, Red, Green; Fusion, Red, Red, Green);

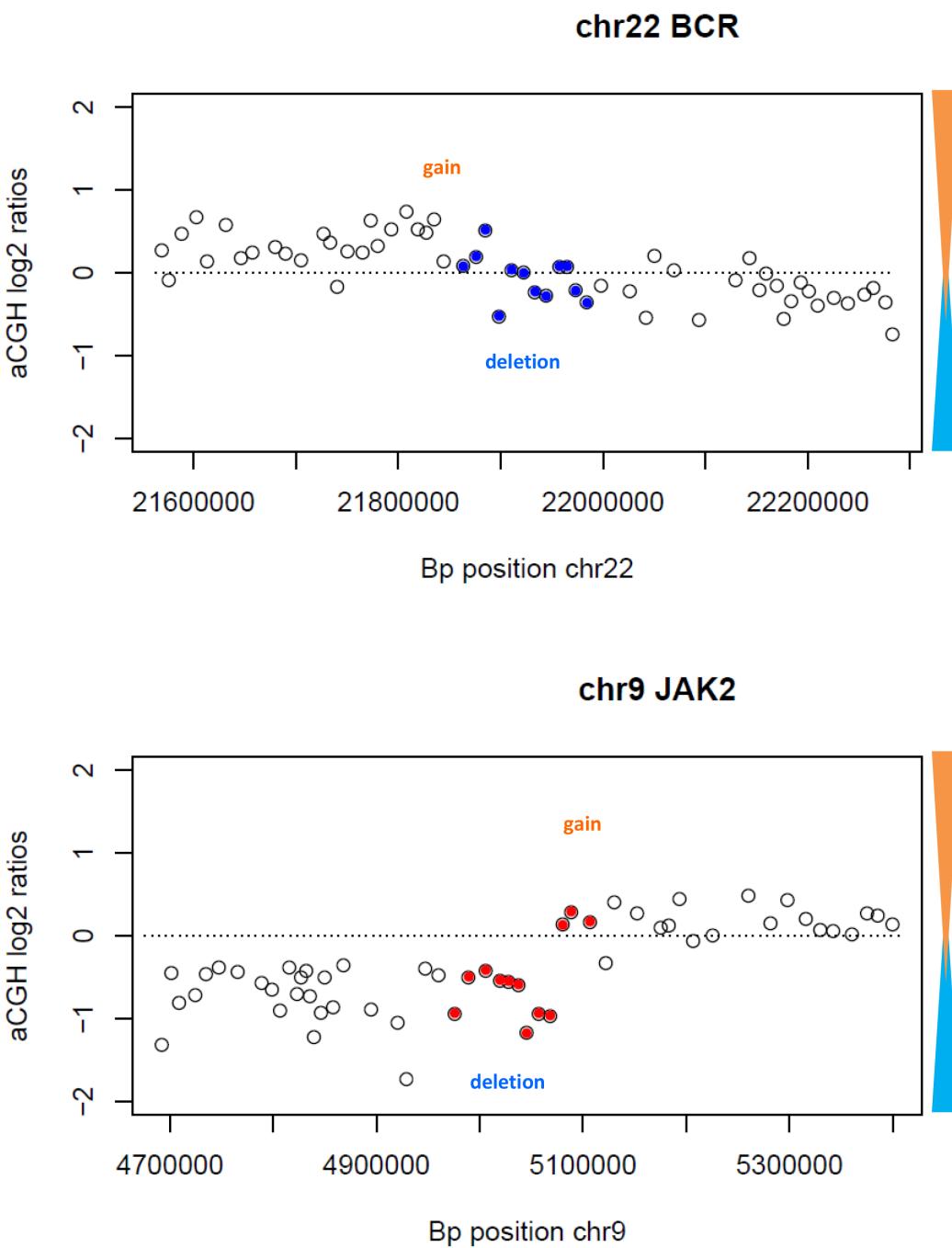
(A) A288 *EBF1-PDGFRB* balanced translocation t(5;5)(B) R32 *EBF1-PDGFRB* intrachromosomal deletion on chromosome 5

(Continued)

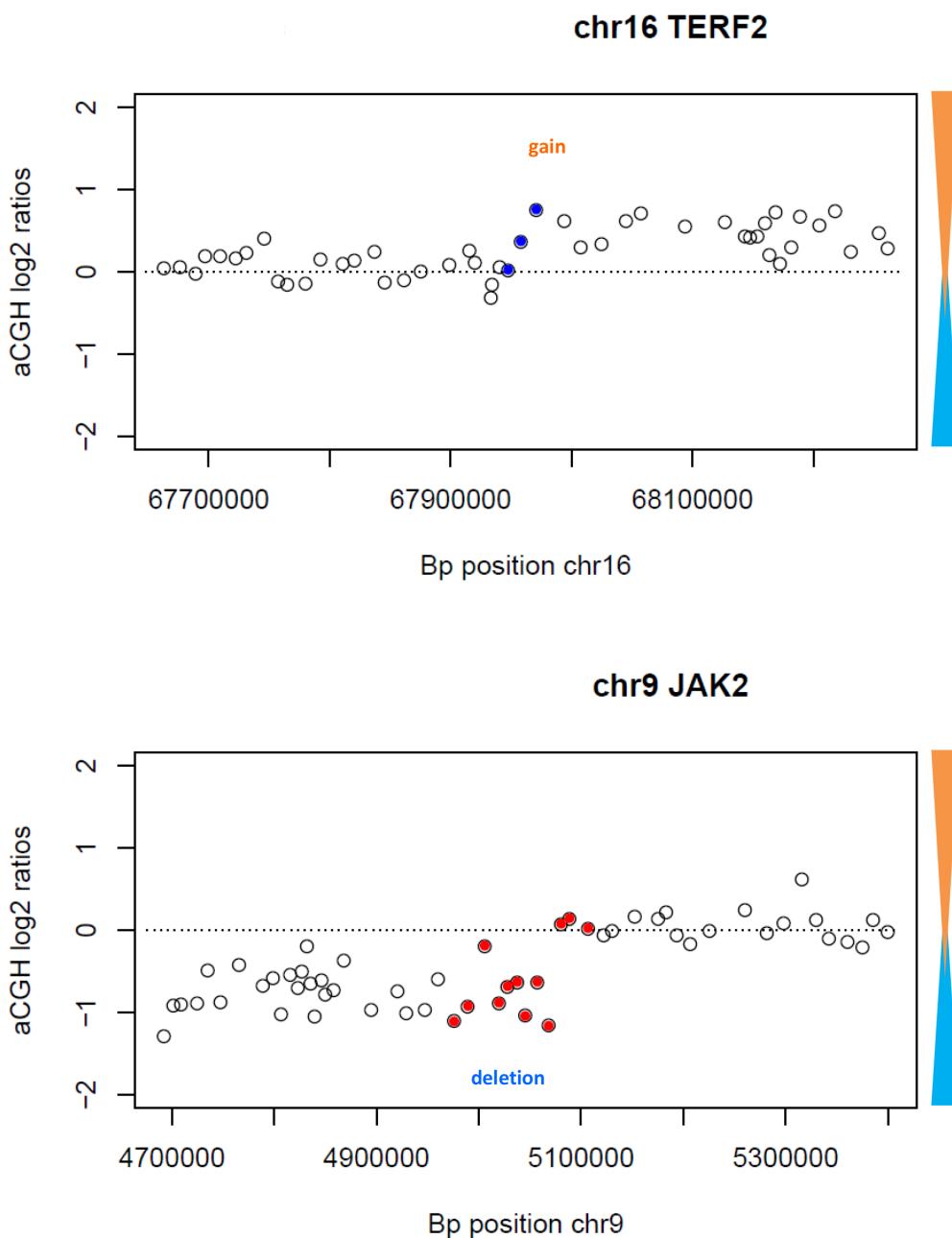
(C) A526 *SSBP2-CSF1R* intrachromosomal duplication on chromosome 5(D) A123 *SSBP2-CSF1R* resulting from chromothripsis of chromosome 5

(Continued)

(E) A216 BCR-JAK2 fusion involving chromosomes 22 and 9



(Continued)

(F) A214 *TERF2-JAK2* fusion involving chromosomes 16 and 9

**Supplementary Figure 5: Array comparative genomic hybridization 180K Agilent array data for tyrosine kinase fusion cases.** The x-axis indicates genomic location on the indicated chromosome, the y-axis shows the called array-CGH data with 0 representing two copies, 1 representing gain and -1 loss A-C. or the normalized log<sub>2</sub> ratios D-F. The colored triangles on the right indicate gain (orange) and loss (blue). (A-D) Rearrangements involving chromosome 5. Beginning and end position of the genes involved in the tyrosine kinase fusions are indicated by colored vertical lines: purple, CSF1R; red, PDGFRB; blue, EBF1; light-blue, SSBP1. The orientation of the genes is indicated with < for minus strand and > plus strand. (E-F) Rearrangements resulting in JAK2 fusions.

**Supplementary Table 1: Overview of the numbers of tested and positive cases for the indicated ABL/JAK class tyrosine kinase fusions**

Tyrosine kinase fusions	<i>BCR-ABL1</i> -like B-other		non- <i>BCR-ABL1</i> -like B-other		Total tested
	tested	positive	tested	positive	
<i>EBF1-PDGFRB</i>	77	4	76		153
<i>NUP214-ABL1</i>	77		76		153
<i>RANBP2-ABL1</i>	77		76		153
<i>ETV6-ABL1</i>	77		76		153
<i>RCSD1-ABL1</i>	77		76		153
<i>PAX5-JAK2</i>	77	3	76		153
<i>STRN3-JAK2</i>	77		76		153
<i>TNIP1-PDGFRB</i>	51		23		74
<i>ZEB2-PDGFRB</i>	51		23		74
<i>SSBP2-PDGFRB</i>	51		23		74
<i>SNX2-ABL1</i>	51		23		74
<i>RCSD1-ABL2</i>	51	1	23		74
<i>PAG1-ABL2</i>	51		23		74
<i>ZC3HAV1-ABL2</i>	51		23		74
<i>SSBP2-CSF1R</i>	51	1	23		74
<i>EBF1-CSF1R</i>	51		23		74
<i>ATF7IP-JAK2</i>	51		23		74
<i>EBF1-JAK2</i>	51		23		74
<i>ETV6-JAK2</i>	51		23		74
<i>PPFIBP-JAK2</i>	51		23		74
<i>SSBP2-JAK2</i>	51		23		74
<i>TPR-JAK2</i>	51		23		74
<i>MYH9-IL2RB</i>	51		23		74
<i>MYB-TYK2</i>	51		23		74
<i>TERF2-JAK2</i>	50	1	23		73
<i>ZMIZ1-ABL1</i>	48	1	23		71
<i>PAG1-ABL1</i>	47		23		70
<i>ZC3HAV1-ABL1</i>	47		23		70
<i>NUP214-ABL2</i>	47		23		70
<i>RANBP2-ABL2</i>	47		23		70
<i>ETV6-ABL2</i>	47		21		68
<i>SNX2-ABL2</i>	47		19		66
<i>BCR-JAK2</i>	46	1	23		69
<i>ZMIZ1-ABL2</i>	44		19		63
<i>TNIP1-PDGFRB</i>	43		13		56
<i>ZEB2-PDGFRB</i>	43		13		56
<i>EBF1-CSF1R</i>	43		15		58
<i>BCR-ABL1</i> (p190)	43		13		56
<i>ETV6-NTRK3</i>	31		22		53
<i>FOXPI-ABL1</i>	19	1	1		20

**Supplementary Table 2: Reverse transcription PCR primers used for the detection of tyrosine kinase fusion genes**

See Supplementary File 1

**Supplementary Table 3: Overview of tyrosine kinase fusion detection on patient cohort**

See Supplementary File 2

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